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Running Title: PCBs, Dietary Fat and Atherosclerosis

Key Words: dietary fat; PCB; lipid metabolism; gene expression; vascular endothelial cells; atherosclerosis

Abbreviations used: LDL-R, low density lipoprotein receptor; PCB, polychlorinated biphenyls; VCAM-1, vascular cell adhesion molecule-1; ROS, reactive oxidative species; BHT, butylated hydroxytoluene; BF₃, boron trifluoride; GC, gas chromatography; PBS, phosphate buffered saline; RNA, ribonucleic acid; RT-PCR, reverse transcription-polymerase chain reaction; CYP, cytochrome P450; SOD, superoxide dismutase; CPT, carnitine palmitoyltransferase; IL-6, interleukin-6;

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1 **ABSTRACT**

2 There is evidence that dietary fat can modify the cytotoxicity of polychlorinated
3 biphenyls (PCBs), and that coplanar PCBs can induce inflammatory processes critical in the
4 pathology of vascular diseases. To test the hypothesis that the interaction of PCBs with dietary
5 fat are dependent on the type of fat, LDL-R^{-/-} mice were fed diets enriched either with olive oil
6 or corn oil for 4 weeks. Half of the animals from each group were injected with PCB 77.
7 VCAM-1 expression in aortic arches was non-detectable in the olive oil-fed mice, but was highly
8 expressed in the presence of the PCB. PCB-treatment increased liver neutral lipids and
9 decreased serum fatty acid levels only in mice fed the corn oil-enriched diet. PCB treatment
10 increased mRNA expression of genes involved in inflammation, apoptosis and oxidative stress in
11 all mice. Upon PCB treatment, mice in both olive and corn oil diet groups showed induction of
12 genes involved in fatty acid degradation, however, with the upregulation of different key
13 enzymes. Genes involved in fatty acid synthesis were only reduced upon PCB treatment in corn
14 oil-fed mice, whereas lipid transport/export genes were altered in olive-oil fed mice. These data
15 suggest that dietary fat can modify changes in lipid metabolism induced by PCBs in serum and
16 tissues. These findings have implications for understanding the interactions of nutrients with
17 environmental contaminants on the pathology of inflammatory diseases such as atherosclerosis.